

Letters to the Editor . . .

Undesirable Use of Magnesium Intravenously in Parathion Poisoning

In the September issue of CALIFORNIA MEDICINE (71:250, 1949), the suggested treatment of parathion poisoning includes use of magnesium sulfate, 10 to 20 cc. of 10 per cent solution intravenously, to counteract muscular excitability due to overstimulation of the receptive substance (or myoneural junction) resulting from the parathion. I should like to warn against the free and general use as antidote of magnesium sulfate intravenously by inexperienced physicians, because if the atropine, which is directed to be used conjointly, does not arrest the muscular excitability, the magnesium would probably have to be used in doses which might cause respiratory or cardiac failure or both. Pharmacologically it is well known that magnesium depression of the respiration is accompanied by cardiac depression or failure; in fact, use of this ion intravenously is a favorite painless method of dispatching experimental animals. It is also well known that unless calcium chloride is injected intravenously to combat depression, death occurs promptly. At death, evidences of curarization of the skeletal and diaphragmatic muscles are usually lacking, thus indicating the unreliability of magnesium for depression of the receptive substance in mammals.

There is also chemical evidence to indicate that magnesium is useless or unreliable, or even dangerous, for systemic use in man. Apparently, elimination keeps pace with absorption of small or medium doses which would make it practically useless. The blood concentration of magnesium for a desired grade of depression is seemingly not easy to maintain unless the dosage is relatively high. This was indicated by the experimental results of Neuwirth and Wallace 20 years ago (J. Pharm. Exp. Therap., 35:171, 1929). These authors showed that the normal serum concentration of 1.0 to 2.0 mg. per cent could be increased to 3.0 mg. per cent without depression after giving rather large doses intramuscularly (0.25 gm. per kg., equivalent to 7.5 gm. for a 70 kg. adult), but it was necessary to raise it to 5.0 mg. per cent to give evidences of depression, which became severe to grave at 20.0 to 23.0 mg. per cent. However, commonly used analgesic doses in human individuals produced less than 4.0 mg. per cent. These blood levels and the various effects mentioned indicate that the margin of safety for magnesium systemically is too narrow to warrant its use in man, whether its salts are used intravenously or intramuscularly. I may add that whenever the systemic use of magnesium is contemplated, calcium chloride solution (500 cc. or so of 0.02 per cent) should be ready at hand for intravenous injection,

as this is a specific antidote against both respiratory and cardiac depression of the magnesium ion.

If the twitchings or convulsions of parathion are serious enough to require checking, probably better and safer than magnesium intravenously would be the use of d-tubocurarine chloride (N.N.R.) intramuscularly, or intravenously for rapid effect. The initial dose of this drug may be 0.15 mg. per kg. body, or somewhat less (total about 6.0 to 9.0 mg. as against a calculated total of 10.5 mg. for a 70 kg. adult), and an additional total of about 3.0 mg. may be given in about five minutes and repeated if necessary. Of course, ready at hand must be means for giving artificial respiration or oxygen inhalation and injecting physostigmine or neostigmine methyl sulfate to combat sudden respiratory reduction or arrest. Fortunately, d-tubocurarine usually paralyzes the receptive substance of the peripheral skeletal muscles first and of the diaphragm last, but it does not depress the respiratory center or heart directly. Thus, prompt combating of any anoxia usually maintains the functional integrity of these two organs. The patient should be hospitalized for this treatment, as he probably would be anyway when poisoned severely. Minor excitation could probably be better checked with soluble pentobarbital or phenobarbital injected intramuscularly.

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Neomycin

One of the handicaps to the use of streptomycin in the treatment of tuberculosis arises from the development of streptomycin-resistant strains of the tubercle bacillus. In hope of finding an antibiotic effective against such streptomycin-resistant strains, Waksman¹ and his associates of Rutgers University tested filtrates from a thousand cultures of soil bacteria. *In vitro* tests showed that several of these filtrates were effective bacteriostatic agents. Most of them, however, were too toxic or unstable to be of therapeutic interest. Recently, however, a non-toxic stable filtrate has been found, from which a new antibiotic "Neomycin" has been isolated.

Neomycin can be separated from a fluid culture by routine methods of adsorption and elution, but has not yet been obtained in crystalline form. It is thermostable, soluble in water, but insoluble in organic solvents. It is equal or superior to streptomycin and streptothricin in its *in vitro* bacteriostatic action against a wide range of Gram-positive and Gram-negative bacteria. Against laboratory strains of *Staphylococcus aureus*, for example, it is ten times more effective than streptomycin, and of a three times higher bacteriostatic titer than strepto-